```
********** Welcome to STN International ******
****

 NEWS 1       Web Page URLs for STN Seminar Schedule - N.
America
 NEWS 2       "Ask CAS" for self-help around the clock
 NEWS 3 FEB 25 CA/CAPLUS - Russian Agency for Patents and
Trademarks          (ROSPATENT) added to list of core patent
offices covered
 NEWS 4 FEB 28 PATDPAFULL - New display fields provide for
legal status          data from INPADOC
 NEWS 5 FEB 28 BABS - Current-awareness alerts (SDIs)
available
 NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded
 NEWS 7 MAR 02 GBFULL: New full-text patent database on
STN
 NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence
annotations enhanced
 NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER
reloaded
 NEWS 10 MAR 22 KOREAPAT now updated monthly; patent
information enhanced
 NEWS 11 MAR 22 Original IDE display format returns to
REGISTRY/ZREGISTRY
 NEWS 12 MAR 22 PATDPASPC - New patent database available
 NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with
experimental property tags
 NEWS 14 APR 04 EPFULL enhanced with additional patent
information and new          fields
 NEWS 15 APR 04 EMBASE - Database reloaded and enhanced
 NEWS 16 APR 18 New CAS Information Use Policies available
online
 NEWS 17 APR 25 Patent searching, including current-
awareness alerts (SDIs),          based on application date in
CA/CAplus and USPATFULL/USPAT2          may be affected by
a change in filing date for U.S.          applications.

 NEWS EXPRESS JANUARY 10 CURRENT WINDOWS VERSION IS
V7.01a, CURRENT          MACINTOSH VERSION IS V6.0c(ENG)
AND V6.0Jc(JP),          AND CURRENT DISCOVER FILE IS DATED
10 JANUARY 2005

 NEWS HOURS   STN Operating Hours Plus Help Desk Availability
 NEWS INTER   General Internet Information
 NEWS LOGIN   Welcome Banner and News Items
 NEWS PHONE   Direct Dial and Telecommunication Network
Access to STN
 NEWS WWW     CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news
on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement. Please note that this agreement limits use to
scientific
  research. Use for software development or design or
implementation
  of commercial gateways or other similar uses is prohibited and
may
  result in loss of user privileges and other penalties.

  ********** STN Columbus **********
****

FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005

=> file caplus
COST IN U.S. DOLLARS                    SINCE FILE
TOTAL                                 ENTRY   SESSION
FULL ESTIMATED COST                    0.21      0.21

FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER
AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field
(available
for records published or updated in Chemical Abstracts after
December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in
searching
databases on STN. Any dissemination, distribution, copying, or
storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 27 Apr 2005  VOL 142 ISS 18
FILE LAST UPDATED: 26 Apr 2005  (20050426/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for
details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> hcv/bi,ab
HCV IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the
system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s hcv/bi,ab      9043 HCV/BI                 8595 HCV/AB
L1        9043 HCV/BI,AB

=> s (hepatitis(w)c)/bi,ab     47012 HEPATITIS/BI
37966 HEPATITIS/AB              3296295 C/BI
3126291 C/AB
L2        13330 (HEPATITIS(W)C)/BI,AB

=> s l1 or l2
L3        13947 L1 OR L2

=> s odn3/bi,ab       10 ODN3/BI                  8 ODN3/AB
L4          10 ODN3/BI,AB

=> s oligonucleotide#/bi,ab     75023 OLIGONUCLEOTIDE#/BI
57855 OLIGONUCLEOTIDE#/AB
L5        75023 OLIGONUCLEOTIDE#/BI,AB

=> s oligodeoxynucleotide#/bi,ab      7363
OLIGODEOXYNUCLEOTIDE#/BI                6256
OLIGODEOXYNUCLEOTIDE#/AB
L6        7363 OLIGODEOXYNUCLEOTIDE#/BI,AB
```

=> s oligodeoxyribonucleotide#/bi,ab 9483
OLIGODEOXYRIBONUCLEOTIDE#/BI 3493
OLIGODEOXYRIBONUCLEOTIDE#/AB
L7 9483 OLIGODEOXYRIBONUCLEOTIDE#/BI,AB

=> s l4 or l5 or l6 or l7
L8 82587 L4 OR L5 OR L6 OR L7

=> s l3 and l8
L9 596 L3 AND L8

=> s antisense/bi,ab 38114 ANTISENSE/BI 26530
ANTISENSE/AB
L10 38114 ANTISENSE/BI,AB

=> s (anti(w)sense)/bi,ab 366044 ANTI/BI 288753
ANTI/AB 35564 SENSE/BI 34004
SENSE/AB
L11 1297 (ANTI(W)SENSE)/BI,AB

=> s l10 or l11
L12 38918 L10 OR L11

=> s l8 and l12
L13 19463 L8 AND L12

=> s l9 and l12
L14 166 L9 AND L12

=> s l14 not 2005/py 341973 2005/PY
L15 136 L14 NOT 2005/PY

=> s l15 not 2004/py 1195310 2004/PY
L16 99 L15 NOT 2004/PY

=> s l16 not 2003/py 1230298 2003/PY
L17 82 L16 NOT 2003/PY

=> s l17 not 2002/py 1161634 2002/PY
L18 66 L17 NOT 2002/PY

=> s l18 not 2001/py 1103342 2001/PY
L19 49 L18 NOT 2001/PY

=> s l19 not 2000/py 1030820 2000/PY
L20 38 L19 NOT 2000/PY

=> s l20 not 1999/py 934329 1999/PY
L21 27 L20 NOT 1999/PY

=> s l21 not 1998/py 906901 1998/PY
L22 18 L21 NOT 1998/PY

=> d his
(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005
L1 9043 S HCV/BI,AB
L2 13330 S (HEPATITIS(W)C)/BI,AB
L3 13947 S L1 OR L2
L4 10 S ODN3/BI,AB
L5 75023 S OLIGONUCLEOTIDE#/BI,AB
L6 7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7 9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB
L8 82587 S L4 OR L5 OR L6 OR L7
L9 596 S L3 AND L8
L10 38114 S ANTISENSE/BI,AB
L11 1297 S (ANTI(W)SENSE)/BI,AB
L12 38918 S L10 OR L11
L13 19463 S L8 AND L12
L14 166 S L9 AND L12
L15 136 S L14 NOT 2005/PY
L16 99 S L15 NOT 2004/PY
L17 82 S L16 NOT 2003/PY
L18 66 S L17 NOT 2002/PY
L19 49 S L18 NOT 2001/PY
L20 38 S L19 NOT 2000/PY
L21 27 S L20 NOT 1999/PY
L22 18 S L21 NOT 1998/PY

=> d l22 1-18 bib ab

L22 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:415321 CAPLUS
DN 129:240824
TI Inhibition of ***hepatitis*** ***C*** virus by ***antisense*** ***oligodeoxynucleotide*** in vitro
AU Liu, Yong; Chen, Zhi; He, Nanxiang; Liu, Kezhou; Zhang, Mingtai; Wang, Xinzi
CS Institute of Infectious Disease, Zhejiang Medical University, Hangzhou, 310003, Peop. Rep. China
SO Zhonghua Yixue Zazhi (1997), 77(8), 567-570 CODEN: CHHTAT; ISSN: 0376-2491
PB Zhonghua Yixue Zazhi
DT Journal
LA Chinese
AB The inhibitory effect of ***antisense*** ***oligodeoxynucleotide*** on ***hepatitis*** ***C*** virus (***HCV***) in vitro was studied. The H9 cells transfected by pCD- ***HCV*** , a recombinant ***HCV*** contg. total ***HCV*** structural gene, were treated with 2 15-mers phosphorothioate (PS) ODNs (***oligodeoxynucleotides***) complementary (PS-ASON) and homologous to ***HCV*** core genomic region, which were labeled with digoxin (DIG). Spot blot hybridization was carried out. And, rPS-ODN (a 15-mers PS ODN of random sequence) or PS-ASON, treated by the 2 ODNs, were modified with 2 liposomes (DOTAP and lipofectin) and calcium phosphate pptn. resp. The variation of level of ***HCV*** mRNA and ***HCV*** antigen expression was obsd. by RT-PCR and dot ELISA with a half-ration. PS-ODN and PS-ASON were detected in the H9 cells. The target gene hybridized to PS-ASON and PS-ODN labeled with DIG. Only the ***antisense*** PS-ASON decreased ***HCV*** mRNA and ***HCV*** antigen expression levels. PS-ODN and rPS-ODN, however, were not effective. The time-dependent and dose-dependent inhibition of PS-ASON was obsd. Both of liposomal PS-ASON showed more highly effective inhibition, in contrast to free PS-ASON, but calcium phosphate pptn.-PS-ASON complex did not. PS-ASON did not influence the H9 cells growth at 10 .mu.mol L-1. PS-ASON complementary to ***HCV*** core gene is asODN and exerts ***antisense*** -inhibitory effect on the level of ***HCV*** translation obviously, but not on the level of ***HCV*** replication and transcription.

L22 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:758344 CAPLUS
DN 128:84071
TI Backbone modified ***antisense*** ***oligodeoxynucleotides*** directed against the ***hepatitis*** - ***C*** -virus (***HCV***)-RNA
AU Eisenhardt, S.; Samstag, W.; Jahn-Hofman, K.; Engels, J. W.; Renz, R.; Hofschneider, P. H.; Caselmann, W. H.; Alt, M.

CS Institute for Organic Chemistry, Johann Wolfgang-University of Frankfurt, Germany
SO Nucleosides & Nucleotides (1997), 16(7-9), 1669-1672 CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB We synthesized 23-mer ***oligodeoxynucleotides*** (ODN's) with different modifications, directed against nt 326-348 of ***HCV*** -RNA. The ODN contains 6 modified nucleotides. The types of modification we tested are nonionic (methylphosphonates, benzylphosphonates) and ionic phosphothioates.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:295885 CAPLUS
DN 127:28649
TI Core specific ***antisense*** phosphorothioate ***oligodeoxynucleotides*** as potent and specific inhibitors of ***hepatitis*** ***C*** viral translation
AU Alt, M.; Renz, R.; Hofschneider, P. H.; Caselmann, W. H.
CS Department of Virus Research, Max-Planck-Institut fur Biochemie, Martinsried, Germany
SO Archives of Virology (1997), 142(3), 589-599 CODEN: ARVIDF; ISSN: 0304-8608
PB Springer
DT Journal
LA English
AB ***Antisense*** phosphorothioate ***oligodeoxynucleotides*** (S-ODN) complementary to sequence stretches in the 5' non-coding region (NCR) of the ***hepatitis*** ***C*** virus (***HCV***) have recently been shown to effectively inhibit viral gene expression. In order to further delineate the optimum target region in the highly conserved 5' end of the viral RNA, S-ODN 5, complementary to ***HCV*** core coding sequences were analyzed in the present study. In a rabbit reticulocyte lysate (RRL) in vitro translation assay S-ODN 5, complementary to the ***HCV*** -RNA nucleotides 340-353, and S-ODN-6, complementary to nucleotides 348-365, resulted in an inhibition of viral translation of 90.4 .+-. 1.3% and 93.7 .+-. 5.1%, resp. at a concn. of 4.14 .mu.M. S-ODN 7, complementary to nucleotides 371-388, was relatively inefficient and showed a maximal inhibition of 42.4 .+-. 12.2%. It has been suggested that in living cells an inhibition by S-ODN is mainly mediated by the action of RNAse H. In RRL the RNAse H content is very low; therefore, to simulate the situation in living cells inhibition expts. in RRL enriched with RNAse H were performed. Under these conditions S-ODN 5, 6 and 7 inhibited viral translation by 45.6 .+-. 6.3%, 80.3 .+-. 2.8% and 70.9 .+-. 5.7% at concns. as low as 0.2 .mu.M. At this concn. no inhibition was obsd. in the std. RRL assay. In cell culture S-ODN 7 was by far the most efficient inhibitor of viral translation, resulting in a specific inhibition of 89.4 .+-. 3.6% at a concn. of 0.3 .mu.M. Taken together with the results of our previous study, nucleotides 326-348 comprising the 3' end of the NCR and nucleotides 371-388, located entirely in the core coding region of the ***HCV*** RNA, are effective targets for S-ODN mediated inhibition of viral translation.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:35883 CAPLUS
DN 126:153311
TI Combinatorial screening and rational optimization for hybridization to folded ***hepatitis*** ***C*** virus RNA of ***oligonucleotides*** with biological ***antisense*** activity
AU Lima, Walt F.; Brown-Driver, Vickie; Fox, Maureen; Hanecak, Ronnie; Bruice, Thomas W.
CS Dep. Res. Med. Chem., Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Journal of Biological Chemistry (1997), 272(1), 626-638 CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB We describe our initial application of a biochem. strategy, comprising combinatorial screening and rational optimization, which directly identifies ***oligonucleotides*** with max. affinity (per unit length), specificity, and rates of hybridization to structurally preferred sites on folded RNA, to the problem of design of ***antisense*** ***oligonucleotides*** active against the ***hepatitis*** ***C*** virus (***HCV***). A fully randomized sequence DNA ***oligonucleotide*** (10-mer) library was equilibrated with each of two folded RNA fragments (200 and 370 nucleotides (nt)), together spanning the 5' 440 nt of an ***HCV*** transcript (by overlapping 130 nt), which were varied over a range of concns. The equilibrations were performed in soln. under conditions detd. to preserve RNA structure and to limit all RNA-DNA library ***oligonucleotide*** interactions to 1:1 stoichiometry. Subsequent Escherichia coli RNase H (endoribonuclease H: EC 3.1.26.4) cleavage anal. identified two preferred sites of highest affinity heteroduplex hybridization. The lengths and sequences of different substitute chem. ***oligonucleotides*** complementary to these sites were rationally optimized using an iterative and quant. anal. of binding affinity and specificity. Thus, DNA ***oligonucleotides*** that hybridized with the same affinity to the preferred sites in the folded RNA fragments found by screening as to short (.ltoreq.25 nt) RNA complements were identified but were found to vary in length (10-18 nt) from site to site. Phosphorothioate (P=S) and 2'-fluoro (2'-F) uniformly substituted ***oligonucleotides*** also were found, which hybridized optimally to these sites, supporting the design of short (10-15-nt) and maximally specific ***oligonucleotides*** that are more nuclease-resistant (via P=S) and have higher affinity (via 2'-F) than DNA. Finally, the affinities of DNA and uniform 2'-F-, P=S-substituted 10-20-mer ***oligonucleotide*** complements for the best hybridization site, from ***HCV*** nt 355 to nt 364-374, closely corresponded to ***antisense*** mechanism inhibition activities in an in vitro translation assay and in a human cell-based ***HCV*** core protein expression assay, resp. These results validate our strategy for the selection of hybridization-optimized and biol. active ***antisense*** ***oligonucleotides*** targeting ***HCV*** RNA and support the potential for utility in further applications.
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:609713 CAPLUS
DN 125:240209
TI PCR-based methods for detecting positive or negative strand of RNA virus
IN Yamaguchi, Kenjiro; Matsunaga, Yuka; Fukutani, Toyoji
PA Tonen Corp, Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE
PI JP 08187097 A2 19960723 JP 1994-338535 19941228
PRAI JP 1994-338535 19941228
AB A method for detecting the pos. or neg. strand of a RNA virus comprises enzymic synthesizing the cDNA using ***antisense*** or sense primers. The method can be applied in the detection of the pos. and neg. strand RNA of ***hepatitis*** ***C*** virus (***HCV***). Both sense and ***antisense*** primer for detecting ***HCV*** RNA are provided. The method can be used for monitoring the interferon (IFN) treatment for ***HCV*** infection.

L22 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:607254 CAPLUS
DN 125:240208
TI ***Hepatitis*** ***C*** virus genotype determination by PCR-based methods
IN Yamaguchi, Kenjiro; Hasegawa, Akira
PA Tonen Corp, Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE
PI JP 08187096 A2 19960723 JP 1994-309865 19941118
PRAI JP 1994-309865 19941118
AB A PCR-based method for the detn. of ***hepatitis*** ***C*** virus (***HCV***) genotypes by targeting the conserved 5' UTR region is described. The method comprises (1) amplification of its 5' UTR region encompassing residues 117.apprx.120 and (2) digestion of the PCR products with HaeIII. Two sets of ***oligonucleotide*** primers are provided for PCR. The method is more sensitive the prior arts (e.g. the Okamoto method). The method can be used for monitoring the treatment using interferon (IFN).

L22 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:604352 CAPLUS
DN 125:292323
TI In vitro inhibition of ***hepatitis*** ***C*** virus gene expression by chemically modified ***antisense*** oligodeoxynuceolotides
AU Vidalin, O.; Major, M. E.; Rayner, B.; Imbach, J.-L.; Trepo, C.; Inchauspe, G.
CS Institut National de la Sante, la Recherche Medicale U271, Lyon, 69424, Fr.
SO Antimicrobial Agents and Chemotherapy (1996), 40(10), 2337-2344 CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
AB The authors have explored different domains within the ***hepatitis*** ***C*** virus (***HCV***) 5' noncoding region as potential targets for inhibition of ***HCV*** translation by ***antisense*** ***oligodeoxynucleotides*** (ODNs). Inhibition assays were performed with two different cell-free systems, rabbit reticulocyte lysate and wheat germ ext., and three types of chem. structures for the ODNs were evaluated: natural phosphodiesters (.beta.-PO), .alpha.-anomer phosphodiesters (.alpha.-PO), and phosphorothioates (PS). A total of six original ODNs, displaying sequence-specific inhibition ranging from 62 to 96%, that mapped in the pyrimidine-rich tract (nucleotides [nt] 104 to 127) and in the initiator AUG codon (nt 338 to 357) were identified. Two ODNs, which were targeted at the initiatory AUG (nt 341 to 367 and 351 to 377) and which had been previously described as active against genotype 1b and 2a sequences, were shown to exhibit inhibition of expression (>95%) of a type 1a sequence. Control expts. with the irrelevant chloramphenicol acetyltransferase sequence as a marker and randomized ODNs demonstrated that levels of inhibition assocd. with the use of PS compds. (or as much as 94%) were mainly due to nonspecific effects. Both .alpha.- and .beta.-PO ODNs were found equally active, and no difference could be seen in the activity of .beta.-PO when it was tested in either rabbit reticulocyte lysate or wheat germ ext., suggesting that RNase H-independent mechanisms may be involved in the inhibitions obsd. However, specific RNA cleavage products generated from .beta.-PO inhibition expts. could be identified, indicating that, with these compds., control of translation also involves RNase H-dependent mechanisms. This study further delimits the existence of favorable target sequences for the action of ODNs within the ***HCV*** 5' noncoding region and indicates the possibility of using nuclease-resistant .alpha.-PO compds. in cellular studies.

L22 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:484299 CAPLUS
DN 125:213586
TI Characterization of cell lines allowing tightly regulated expression of ***hepatitis*** ***C*** virus core protein
AU Moradpour, Darius; Englert, Christoph; Wakita, Takaji; Wands, Jack R.
CS Molecular Hepatology Lab., Harvard Medical Sch., Charlestown, MA, 02129, USA
SO Virology (1996), 222(1), 51-63 CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB A tetracycline-regulated system was used to generate cell lines allowing tightly controlled expression of a ***hepatitis*** ***C*** virus (***HCV***) cDNA comprising the 5' noncoding, the core, and part of the E1 regions. Prodn. of 21-kDa processed nucleocapsid protein could be regulated over a broad range by the concn. of tetracycline present in the culture medium. Induction ratios of over 1000-fold were found using an ***HCV*** core-luciferase fusion construct. Core protein had an intracellular half-life of 9 h and corresponded to the product of 173 amino-terminal amino acids of the ***HCV*** open reading frame. Sequential immunofluorescence microscopy revealed the presence of core antigen first in a predominantly perinuclear fine-reticular staining pattern and subsequently also in cytoplasmic granules and vesicles. By immunoelectron microscopy core protein was found on the endoplasmic reticulum membrane and on the surface of cytoplasmic lipid droplets. Growth rate analyses and colony formation efficiency assays showed no major cytotoxic effect of ***HCV*** core protein expression per se. ***HCV*** gene expression could be inhibited by an ***antisense*** ***oligonucleotide*** targeting a region immediately downstream of the translation initiation codon. These cell lines represent important tools to investigate structural and functional properties of ***HCV*** core protein and may be useful to evaluate gene therapeutic strategies against ***HCV*** in a cellular system.

L22 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:433085 CAPLUS
DN 125:159621
TI ***Antisense*** ***oligonucleotide*** inhibition of ***hepatitis*** ***C*** virus gene expression in transformed hepatocytes
AU Hanecak, Ronnie; Brown-Driver, Vickie; Fox, Maureen C.; Azad, Raana F.; Furusako, Shoji; Nozaki, Chikateru; Ford, Clifford; Sasmor, Henri; Anderson, Kevin P.
CS Department Infectious Diseases, Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Journal of Virology (1996), 70(8), 5203-5212 CODEN: JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Genetic and biochem. studies have provided convincing evidence that the 5' noncoding region (5' NCR) of ***hepatitis*** ***C*** virus (***HCV***) is highly conserved among viral isolates worldwide and that translation of ***HCV*** is directed by an internal ribosome entry site (IRES) located within the 5' NCR. We have investigated inhibition of ***HCV*** gene expression using ***antisense*** ***oligonucleotides*** complementary to the 5' NCR, translation initiation codon, and core protein coding sequences. ***Oligonucleotides*** were evaluated for activity after treatment of a human hepatocyte cell line expressing the ***HCV*** 5' NCR, core protein coding sequences, and the majority of the envelope gene (E1). More than 50 ***oligonucleotides*** were evaluated for inhibition of ***HCV*** RNA and protein expression. Two ***oligonucleotides*** , ISIS 6095, targeted to a stem-loop structure within the 5' NCR known to be important for IRES function, and ISIS 6547, targeted to sequences spanning the AUG used for initiation of ***HCV*** polyprotein translation, were found to be the most effective at inhibiting ***HCV*** gene expression. ISIS 6095 and 6547 caused concn.-dependent redns. in ***HCV*** RNA and protein levels, with 50% inhibitory concns. of 0.1 to 0.2 .mu.M. Redn. of RNA levels, and subsequently protein levels, by these phosphorothioate ***oligonucleotides*** was consistent with RNase H cleavage of RNA at the site of ***oligonucleotide*** hybridization. Chem. modified ***HCV*** ***antisense*** phosphodiester ***oligonucleotides*** were designed and evaluated for inhibition of core protein expression to identify ***oligonucleotides*** and ***HCV*** target sequences that do not require RNase H activity to inhibit expression. A uniformly modified 2'-methoxyethoxy phosphodiester ***antisense*** ***oligonucleotide*** complementary to the initiator AUG reduced ***HCV*** core protein levels as effectively as phosphorothioate ***oligonucleotide*** ISIS 6095 but without reducing ***HCV*** RNA levels. Results of our studies show that ***HCV*** gene expression is reduced by ***antisense*** ***oligonucleotides*** and demonstrate that it is feasible to design ***antisense*** ***oligonucleotide*** inhibitors of translation that do not require RNase H activation. The data demonstrate that chem. modified ***antisense*** ***oligonucleotides*** can be used as tools to identify important regulatory sequences and/or structures important for efficient translation of ***HCV*** .

L22 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:133731 CAPLUS
DN 124:193313
TI Phosphorothioate ***antisense*** ***oligodeoxynucleotides*** capable of inhibiting ***hepatitis*** ***C*** virus gene expression: in vitro translation assay
AU Seki, Makoto; Honda, Yoshikazu
CS Biosciences Laboratory, Mitsubishi Chemical Corporation, Yokohama, 227, Japan
SO Journal of Biochemistry (Tokyo) (1995), 118(6), 1199-204 CODEN: JOBIAO; ISSN: 0021-924X
PB Japanese Biochemical Society
DT Journal
LA English
AB Phosphorothioate ***antisense*** ***oligodeoxynucleotides*** (S-ODNs) designed to hybridize to the 5' region of the ***hepatitis*** ***C*** virus (***HCV***) genome were evaluated as to their ability to inhibit ***HCV*** gene expression, using an in vitro translation system. Three effective regions were found to interfere with the translation of ***HCV*** RNAs. These regions were region A [nucleotides (nt) 124 to 153], region B (nt 100 to 123), and region C (nt 324 to 360). Further detailed evaluation of S-ODNs within each region allowed us to propose some ***HCV*** -specific antiviral agent candidates. Two of them, SMS16 (nt 328 to 347) and SMS17 (nt 326 to 345), caused over 90% inhibition of ***HCV*** gene expression when present in a less than fourfold molar excess; this effect was sequence-specific and dose-dependent.

L22 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:872871 CAPLUS
DN 124:75623
TI Specific inhibition of ***hepatitis*** ***C*** viral gene expression by ***antisense*** phosphorothioate ***oligodeoxynucleotides***
AU Alt, Michael; Renz, Renate; Hofschneider, Peter H.; Paumgartner, Gustav; Caselmann, Wolfgang H.
CS Department Virus Research, Max-Planck-Institut fur Biochemie, Martinsried, 0-82152, Germany
SO Hepatology (Philadelphia) (1995), 22(3), 707-17 CODEN: HPTLD9; ISSN: 0270-9139
PB Saunders
DT Journal
LA English
AB The inhibitory effect of ***antisense*** phosphorothioate ***oligodeoxynucleotides*** (S-ODN) on ***hepatitis*** ***C*** viral gene expression was analyzed in an in vitro test system and in cell culture. S-ODN were directed against different stem loop structures in the 5'noncoding region (NCR) of the ***hepatitis*** ***C*** virus (***HCV***) RNA and against a nucleotide stretch, including the start codon of the polyprotein precursor. The inhibitory effect of these S-ODN was quantified employing a viral RNA consisting of the first 407 nucleotides of a ***HCV*** type 1b genome fused to the coding sequence of the firefly luciferase gene. For in vitro assays, this RNA was generated by in vitro transcription and used as a template in a rabbit reticulocyte lysate in vitro translation system. The prodn. of active luciferase in the absence or presence of S-ODN was monitored using an enzymic assay. The best results were obtained with S-ODN 4 directed against nucleotides 326 to 348, comprising the start AUG of the polyprotein coding sequence. With this ***oligonucleotide*** , a specific and dose-dependent effect was obsd. with a maximal inhibition of 96% at a S-ODN concn. of 4.14 .mu.mol/L. For cell culture expts., the hepatoblastoma cell line HepG2 was transfected with a plasmid expressing the ***HCV*** -luciferase fusion RNA. In this assay system S-ODN 2, complementary to nucleotides 264 to 282 of the ***HCV*** RNA, and S-ODN 4 were most efficient and reduced the viral

translation by 96% and 94%, resp., at a concn. of 0.3 .mu.mol/L. The inhibition was specific (1) because the expression of the ***HCV*** -luciferase fusion RNA was not significantly impaired by the control S-ODN and (2) because the expression of an unrelated mRNA was not or only slightly downregulated. These data suggest that ***HCV*** gene expression can be inhibited effectively by ***antisense*** S-ODN. Therefore, this approach represents a promising perspective for the treatment of ***hepatitis*** ***C*** .

L22 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:718559 CAPLUS
DN 123:160158
TI Inhibition of ***hepatitis*** ***C*** virus replication by ***antisense*** ***oligonucleotide*** in culture cells
AU Mizutani, Tetsuya; Kato, Nobuyuki; Hirota, Masami; Sugiyama, Kazuo; Murakami, Akira; Shimotohno, Kunitada
CS Virol. Div., Natl. Cancer Cent. Res. Inst., Tokyo, 104, Japan
SO Biochemical and Biophysical Research Communications (1995), 212(3), 906-11 CODEN: BBRCA9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB ***Oligonucleotides*** complementary to the sequences contg. the initiator codon, AUG, of the core region of pos.-stranded ***hepatitis*** ***C*** virus (***HCV***) were tested for their effects on viral translation in a cell-free protein synthesis system and on viral replication. Treatment of ***HCV*** -infected MT-2C cells with the ***antisense*** ***oligonucleotide*** (10 .mu.M) had a dramatic inhibitory effect on viral replication. This result suggests that the ***antisense*** ***oligonucleotide*** complementary to the sequence close to the initiation codon of the core region might be useful as an antiviral agent against ***HCV*** replication.

L22 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:450837 CAPLUS
DN 122:206941
TI Pestivirus translation initiation occurs by internal ribosome entry
AU Poole, Toni L.; Wang, Changyu; Popp, R. A.; Potgieter, L. N. D.; Siddiqui, Aleem; Collett, Marc S.
CS Oak Ridge Natl. Lab., Biol. Div., Oak Ridge, TN, 37831, USA
SO Virology (1995), 206(1), 750-4 CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB The role of the 385 nucleotide 5' noncoding region (NCR) in the translation of the pestivirus genome was investigated. In vitro translation of an RNA transcript contg. the 5' NCR of the bovine viral diarrhea virus (BVDV) genome followed by the coding sequence of the first gene product (p20) of the BVDV large open reading frame resulted in the synthesis of a 20-kDa polypeptide. Results from hybrid-arrest translation studies identified a region involving a predicted RNA stem-loop structure spanning nucleotides 154-216 within the 5' NCR that was important for p20 synthesis. An addnl. inhibitory ***oligonucleotide*** was complementary to the sequence at the base of this stem-loop and encompassed the initiating AUG at nucleotide 386. ***Antisense*** ***oligonucleotides*** both upstream and downstream of those that were inhibitory had no effect on p20 translation. RNA from a dicistronic expression vector in which the BVDV 5' NCR was inserted between two reporter genes. CAT and LUC, showed strong expression of the second (LUC) cistron upon in vitro translation. This expression was dramatically reduced in an analogous construct in which nucleotides 173-236 of the 5' NCR were deleted. Similar results were obtained when RNA from these same vectors was evaluated for expression after transfection into BHK cells. These results suggest that the BVDV 5' NCR contains an internal ribosome entry site for translation initiation. This translational mechanism is similar to that shown for ***hepatitis*** ***C*** virus, further demonstrating the close relationship between viruses of these two genera within the family Flaviviridae.

L22 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:348419 CAPLUS
DN 122:122351
TI Treatment and prevention of chronic viral hepatitis
AU Dusheiko, G. M.
CS Royal Free Hospital and School of Medicine, London, NW2 2Q3, UK
SO Pharmacology & Therapeutics (1995), 65(1), 47-73 CODEN: PHTHDT; ISSN: 0163-7258
PB Elsevier
DT Journal; General Review
LA English
AB A review with 150 refs. Chronic viral hepatitis B, C or D may lead to cirrhosis, hepatocellular failure and hepatocellular carcinoma. The morbidity of these diseases has necessitated a prolonged search for effective therapy. Interferon-.alpha. has been studied widely and remains the mainstay of treatment. Therapy for hepatitis B has now become possible with the demonstration that .alpha.-interferons inhibit hepatitis B virus (HBV) replication and that prolonged therapy can lead to a remission. A no. of other cytokines, including thymosin, are being evaluated. Currently used nucleoside analogs and anti-retroviral therapies used in human immunodeficiency virus infection have not proven useful in chronic hepatitis B. There are a no. of new exptl. nucleoside analogs with activity against HBV. Unfortunately, fialuridine has been assocd. with severe mitochondrial damage and hepatotoxicity. Other stereoisomers may be more active and less toxic, but the potential danger of these drugs indicates that large scale clin. trials should proceed cautiously. Exptl. test systems for the preliminary investigation of antiviral compds. in hepatitis B and C will be required. ***Antisense*** ***oligodeoxyribonucleotides*** may inhibit the expression of the HBV genes. The natural history of ***hepatitis*** ***C*** is uncertain. Therapeutic trials of interferon-.alpha. indicated that a proportion of patients may respond to treatment with this agent. There is most information about 3 mU t.i.w. administered for 6 mo. It is not yet clear whether this dose is optimal. Multivariate anal. of several pretreatment parameters indicate that patients without cirrhosis are more responsive to interferon. The influence of genot.gamma..pi.es of ***hepatitis*** ***C*** is the subject of considerab.LAMBDA.e interest at present. Patients with diverse circulating quasispecies may be less responsive to therapy than those with a single major species. Improved responses have been obsd. in patients with lower levels of circulating ***hepatitis*** ***C*** virus RNA.

L22 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:190377 CAPLUS
DN 122:231892
TI Detection and quantification of ***hepatitis*** ***C*** virus RNA replication in the liver
AU Sakamoto, Naoya; Enomoto, Nobuyuki; Kurosaki, Masayuki; Marumo, Fumiaki; Sato, Chifumi

CS Faculty of Medicine, Tokyo Medical and Dental University, Tokyo, 113, Japan
SO Journal of Hepatology (1994), 20(5), 593-7 CODEN: JOHEEC; ISSN: 0168-8278
DT Journal
LA English
AB To investigate the correlation between the replication of ***hepatitis*** ***C*** virus in liver and the clin. and histopathol. features, the authors detected and quantified plus and minus strands of ***HCV*** -RNA in plasma and in livers of patients with chronic ***hepatitis*** ***C*** by a quant. polymerase chain reaction. RNA was extd. from the plasma and liver tissue of ten patients with biopsy-proven chronic ***hepatitis*** ***C*** . The plus and minus strands of ***HCV*** -RNA were detected by a strand-specific reverse transcription with either sense or ***anti*** - ***sense*** ***oligonucleotide*** primers deduced from the ***hepatitis*** ***C*** virus genome, and a std. ***HCV*** -RNA with an enzyme restriction site was used to quantify the amt. of ***HCV*** -RNA. Both plus and minus strands of ***HCV*** -RNA were detected from the liver tissue of all patients included. The amt. of plus-stranded ***HCV*** -RNA in the liver was 10 times higher than that of minus-stranded ***HCV*** -RNA. Plus-stranded ***HCV*** -RNA was detected in the plasma in all patients, while the minus strand was not detected in any patient. There was a weak correlation between the amt. of both strands of ***HCV*** -RNA in the liver and that of the plus strand in plasma. There was no significant correlation between the amt. of liver ***HCV*** -RNA and serum alanine transaminase and aspartate transaminase levels, or histopathol. findings in the liver. This method of detecting and quantifying liver ***HCV*** -RNA is simple and sensitive; it may be used to detect residual ***hepatitis*** ***C*** virus replication after the disappearance of plasma ***HCV*** -RNA in acute hepatitis or in chronic hepatitis after interferon treatment.

L22 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:317870 CAPLUS
DN 120:317870
TI Specific inhibition of ***hepatitis*** ***C*** virus expression by ***antisense*** ***oligodeoxynucleotides*** . In vitro model for selection of target sequence
AU Wakita, Takaji; Wands, Jack R.
CS Mol. Hepatol. Lab., Harvard Med. Sch., Boston, MA, 02114, USA
SO Journal of Biological Chemistry (1994), 269(19), 14205-10 CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB The effect of sense and ***antisense*** ***oligodeoxynucleotides*** (ODNs) on ***hepatitis*** ***C*** virus (***HCV***) gene expression was studied to det. the role of the highly conserved 5'-untranslated region in the life cycle of the virus. It was found that ***antisense*** ODNs complementary to nucleotides (nt) 38-65, 134-175, and 312-339 in the 5' noncoding region and 341-377 in the core open reading frame efficiently blocked ***HCV*** RNA translation. Overlapping ODNs that differed by only several nucleotides showed substantially different inhibition of ***HCV*** RNA translation. Fine sequence specificity testing at nt positions 351-377 revealed that ODNs as small as a 12-mer (nt 351-363) retained a high degree (80%) of inhibitory activity compared to ODNs of longer sequences. These results suggest that there are three highly specific domains in the 5' noncoding region and a sequence immediately downstream of the ***HCV*** core initiation codon that may be crit. for translation of ***HCV*** RNA. This study also provides an exptl. approach for the selection of target ***HCV*** RNA sequences susceptible to ***antisense*** effects, as well as for definition of functional regions of the genome necessary for viral replication.

L22 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:317330 CAPLUS
DN 120:317330
TI Amplification of RNA virus genome in a single container and its detection
IN Yamaguchi, Kenjiro
PA Tonen Corp, Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---------- ---- -------- ---------- -------
PI JP 06046900 A2 19940222 JP 1992-222184 19920729
PRAI JP 1992-222184 19920729
AB A simplified method with reduced risk of contamination for amplification and detection of RNA virus genome comprises (1) extn. of viral RNA in the presence of protein-degradating enzymes, (2) prepn. of cDNA in the presence of reverse of transcriptase, (3) amplification of the cDNA with PCR using 2 sets of primers, (4) sizing and analyzing the PCR products by agarose electrophoresis. A few sets of sense and ***antisense*** PCR primers are provided for detection of ***hepatitis*** ***C*** virus by this method. By this method, 30 samples/day can be processed.

L22 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:642973 CAPLUS
DN 119:242973
TI ***Antisense*** ***oligonucleotides*** and ribozymes for use in the inhibition of replication of viruses using and RNA intermediate
IN Loss, Peter; Schreier, Peter; Maiss, Edgar; Schneider, Rudolf
PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany; Bayer A.-G.; Hoechst A.-G.
SO Eur. Pat. Appl., 19 pp. CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ---------- ---- -------- ---------- -------
PI EP 558944 A2 19930908 EP 1993-101710 19930204 EP 558944 A3 19940608 R: BE, CH, DE, DK, FR, GB, IT, LI, NL DE 4203441 C1 19931014 DE 1992-4203441 19920206 AU 9332166 A1 19930812 AU 1993-32166 19930202 JP 06090758 A2 19940405 JP 1993-18498 19930205
PRAI DE 1992-4203441 A 19920206
AB Oligoribonucleotides capable of binding to, and inhibiting viral replication that passes through an RNA intermediate, are described for use in improving the resistance of plants to pathogenic viruses. These ***oligonucleotides*** may be ***antisense*** ***oligonucleotides*** or ribozymes capable of recognizing and cleaving these RNA intermediates and they may be encoded on an heterologous virus that has been rendered non-pathogenic or on integrating transforming DNA. Synthetic DNA sequences encoding ribozymes capable of cleaving the RNA of tomato spotted wilt virus were constructed by std. phosphoramidite chem. and expression constructs introduced into

tobacco or potato protoplasts by Agrobacterium-mediated transformation. Transgenic tobacco plants challenged with the virus showed greatly reduced severity of infection and lower titers of viral antigens. The application of the method to animal cells is also demonstrated.

=> e kilkuskie r/au
E1 1 KILKUS STEPHEN P/AU
E2 1 KILKUSHIE ROBERT/AU
E3 0 --> KILKUSKIE R/AU
E4 2 KILKUSKIE R E/AU
E5 5 KILKUSKIE ROBERT/AU
E6 28 KILKUSKIE ROBERT E/AU
E7 1 KILKUSKIE ROBERT EDWARD/AU
E8 1 KILKUSKIE ROBERT L/AU
E9 1 KILKUYAMA SAKAE/AU
E10 1 KILL BETH/AU
E11 1 KILL BLOMHOFF HEIDI/AU
E12 1 KILL CLEMENS/AU

=> s e8
L23 1 "KILKUSKIE ROBERT L"/AU

=> e frank b/au
E1 1 FRANK AUSTEN K/AU
E2 1 FRANK AXEL/AU
E3 51 --> FRANK B/AU
E4 1 FRANK B A/AU
E5 22 FRANK B H/AU
E6 3 FRANK B S/AU
E7 34 FRANK BARBARA/AU
E8 1 FRANK BARRY M/AU
E9 2 FRANK BARRY W/AU
E10 1 FRANK BASIL/AU
E11 1 FRANK BASTIAN/AU
E12 2 FRANK BEATE/AU

=> e frank b l/au
E1 1 FRANK B A/AU
E2 22 FRANK B H/AU
E3 0 --> FRANK B L/AU
E4 3 FRANK B S/AU
E5 34 FRANK BARBARA/AU
E6 1 FRANK BARRY M/AU
E7 2 FRANK BARRY W/AU
E8 1 FRANK BASIL/AU
E9 1 FRANK BASTIAN/AU
E10 2 FRANK BEATE/AU
E11 3 FRANK BENJAMIN/AU
E12 5 FRANK BENJAMIN S/AU

=> e frank bruce/au
E1 9 FRANK BRIGITTA/AU
E2 1 FRANK BRIGITTE/AU
E3 9 --> FRANK BRUCE/AU
E4 83 FRANK BRUCE H/AU
E5 19 FRANK BRUCE HILL/AU
E6 13 FRANK BRUCE L/AU
E7 1 FRANK BRUCE LEONARD/AU
E8 1 FRANK BRUCE S/AU
E9 5 FRANK BRUNO/AU
E10 5 FRANK BRYAN/AU
E11 9 FRANK BRYAN C/AU
E12 1 FRANK BUEHLER/AU

=> s e3 or e6 or e7 9 "FRANK BRUCE"/AU 13 "FRANK BRUCE L"/AU 1 "FRANK BRUCE LEONARD"/AU
L24 23 "FRANK BRUCE"/AU OR "FRANK BRUCE L"/AU OR "FRANK BRUCE LEONARD"/ AU

=> e goodchild j/au
E1 3 GOODCHILD I R/AU
E2 1 GOODCHILD IAN D/AU
E3 13 --> GOODCHILD J/AU
E4 1 GOODCHILD J A/AU
E5 1 GOODCHILD J C/AU
E6 3 GOODCHILD J H/AU
E7 1 GOODCHILD JANE/AU
E8 1 GOODCHILD JIM THOMPSON/AU
E9 61 GOODCHILD JOHN/AU
E10 1 GOODCHILD JOHN E/AU
E11 2 GOODCHILD JONATHAN A/AU
E12 2 GOODCHILD JOSIAH H/AU

=> s e3 or e10 or e9 13 "GOODCHILD J"/AU 1 "GOODCHILD JOHN E"/AU 61 "GOODCHILD JOHN"/AU
L25 75 "GOODCHILD J"/AU OR "GOODCHILD JOHN E"/AU OR "GOODCHILD JOHN"/AU

=> e wolfe j/au
E1 1 WOLFE ILONA/AU
E2 1 WOLFE INGRID/AU
E3 41 --> WOLFE J/AU
E4 5 WOLFE J A/AU
E5 1 WOLFE J ALAN/AU
E6 2 WOLFE J B/AU
E7 65 WOLFE J C/AU
E8 6 WOLFE J D/AU
E9 5 WOLFE J E/AU
E10 17 WOLFE J F/AU
E11 29 WOLFE J H/AU
E12 1 WOLFE J H N/AU

=> s e3
L26 41 "WOLFE J"/AU

=> e wolfe j l/au
E1 1 WOLFE J H N/AU
E2 6 WOLFE J K/AU
E3 2 --> WOLFE J L/AU
E4 32 WOLFE J M/AU
E5 3 WOLFE J N/AU
E6 1 WOLFE J O/AU
E7 161 WOLFE J P/AU
E8 1 WOLFE J PRESTON/AU
E9 3 WOLFE J R/AU
E10 10 WOLFE J R JR/AU
E11 1 WOLFE J S III/AU
E12 2 WOLFE J W/AU

=> s e3
L27 2 "WOLFE J L"/AU

=> e wolfe jia/au
E1 2 WOLFE JESSIE/AU
E2 1 WOLFE JESSIE MINAN/AU
E3 1 --> WOLFE JIA/AU
E4 4 WOLFE JIA L/AU
E5 14 WOLFE JIA LIU/AU
E6 1 WOLFE JOACHIM/AU
E7 1 WOLFE JOANNE/AU

E8 24 WOLFE JOE/AU
E9 1 WOLFE JOEL ZEV/AU
E10 10 WOLFE JOHN/AU
E11 7 WOLFE JOHN A/AU
E12 16 WOLFE JOHN C/AU

=> s e3 or e4 or e5 1 "WOLFE JIA"/AU 4 "WOLFE JIA L"/AU 14 "WOLFE JIA LIU"/AU
L28 19 "WOLFE JIA"/AU OR "WOLFE JIA L"/AU OR "WOLFE JIA LIU"/AU

=> e roberts p c/au
E1 6 ROBERTS P ANN/AU
E2 30 ROBERTS P B/AU
E3 6 --> ROBERTS P C/AU
E4 1 ROBERTS P C B/AU
E5 6 ROBERTS P C T/AU
E6 1 ROBERTS P CHRISTOPHER/AU
E7 41 ROBERTS P D/AU
E8 18 ROBERTS P E/AU
E9 11 ROBERTS P ELAINE/AU
E10 6 ROBERTS P F/AU
E11 6 ROBERTS P G/AU
E12 33 ROBERTS P H/AU

=> s e3
L29 6 "ROBERTS P C"/AU

=> e roberts peter/au
E1 1 ROBERTS PEREDUR J P/AU
E2 2 ROBERTS PERRY L/AU
E3 39 --> ROBERTS PETER/AU
E4 7 ROBERTS PETER A/AU
E5 24 ROBERTS PETER B/AU
E6 9 ROBERTS PETER C/AU
E7 1 ROBERTS PETER C T/AU
E8 1 ROBERTS PETER CLAYTON/AU
E9 2 ROBERTS PETER CLIVE B/AU
E10 1 ROBERTS PETER CLIVE BUCKLEY/AU
E11 2 ROBERTS PETER D/AU
E12 3 ROBERTS PETER F/AU

=> s e3 or e6 or e8 39 "ROBERTS PETER"/AU 9 "ROBERTS PETER C"/AU 1 "ROBERTS PETER CLAYTON"/AU
L30 49 "ROBERTS PETER"/AU OR "ROBERTS PETER C"/AU OR "ROBERTS PETER CLAYTON"/AU

=> e hamlin h a/au
E1 1 HAMLIN GREEN G/AU
E2 2 HAMLIN GREEN GINA/AU
E3 1 --> HAMLIN H A/AU
E4 1 HAMLIN H ALLEN JR/AU
E5 1 HAMLIN H C/AU
E6 2 HAMLIN H F/AU
E7 5 HAMLIN H P/AU
E8 1 HAMLIN H S/AU
E9 1 HAMLIN H SCOTT/AU
E10 2 HAMLIN HENRY A/AU
E11 1 HAMLIN HENRY A JR/AU
E12 1 HAMLIN HERBERT SCOTT/AU

=> s e3 or e4 or e10 or e11 1 "HAMLIN H A"/AU 1 "HAMLIN H ALLEN JR"/AU 2 "HAMLIN HENRY A"/AU 1 "HAMLIN HENRY A JR"/AU
L31 5 "HAMLIN H A"/AU OR "HAMLIN H ALLEN JR"/AU OR "HAMLIN HENRY A"/AU OR "HAMLIN HENRY A JR"/AU

=> e roberts n a/au
E1 1 ROBERTS MYRON S/AU
E2 36 ROBERTS N/AU
E3 37 --> ROBERTS N A/AU
E4 53 ROBERTS N B/AU
E5 5 ROBERTS N E/AU
E6 1 ROBERTS N ELIZABETH/AU
E7 3 ROBERTS N F/AU
E8 19 ROBERTS N J/AU
E9 2 ROBERTS N J JR/AU
E10 16 ROBERTS N K/AU
E11 12 ROBERTS N L/AU
E12 2 ROBERTS N M/AU

=> s e2 or e3 36 "ROBERTS N"/AU 37 "ROBERTS N A"/AU
L32 73 "ROBERTS N"/AU OR "ROBERTS N A"/AU

=> e roberts noel/au
E1 13 ROBERTS NIRA R/AU
E2 1 ROBERTS NKRUMAH LAURA B/AU
E3 7 --> ROBERTS NOEL/AU
E4 26 ROBERTS NOEL A/AU
E5 4 ROBERTS NOEL ALLAN/AU
E6 11 ROBERTS NOEL K/AU
E7 1 ROBERTS NOELLE/AU
E8 34 ROBERTS NORBERT J JR/AU
E9 2 ROBERTS NORM/AU
E10 1 ROBERTS NORMAL B/AU
E11 9 ROBERTS NORMAN/AU
E12 25 ROBERTS NORMAN B/AU

=> s e3 or e4 or e5 7 "ROBERTS NOEL"/AU 26 "ROBERTS NOEL A"/AU 4 "ROBERTS NOEL ALLAN"/AU
L33 37 "ROBERTS NOEL"/AU OR "ROBERTS NOEL A"/AU OR "ROBERTS NOEL ALLAN" /AU

=> e walther d m/au
E1 12 WALTHER D C/AU
E2 1 WALTHER D J/AU
E3 10 --> WALTHER D M/AU
E4 2 WALTHER DAGMAR/AU
E5 1 WALTHER DAGNY/AU
E6 1 WALTHER DANE/AU
E7 2 WALTHER DANE S/AU
E8 1 WALTHER DANE STUART/AU
E9 5 WALTHER DANIEL/AU
E10 5 WALTHER DAVID C/AU
E11 4 WALTHER DEBRA M/AU
E12 8 WALTHER DIEGO/AU

=> s e3 or e11 10 "WALTHER D M"/AU 4 "WALTHER DEBRA M"/AU
L34 14 "WALTHER D M"/AU OR "WALTHER DEBRA M"/AU

=> d his
(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005
L1 9043 S HCV/BI,AB
L2 13330 S (HEPATITIS(W)C)/BI,AB
L3 13947 S L1 OR L2
L4 10 S ODN3/BI,AB
L5 75023 S OLIGONUCLEOTIDE#/BI,AB
L6 7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7 9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB

L8 82587 S L4 OR L5 OR L6 OR L7
L9 596 S L3 AND L8
L10 38114 S ANTISENSE/BI,AB
L11 1297 S (ANTI(W)SENSE)/BI,AB
L12 38918 S L10 OR L11
L13 19463 S L8 AND L12
L14 166 S L9 AND L12
L15 136 S L14 NOT 2005/PY
L16 99 S L15 NOT 2004/PY
L17 82 S L16 NOT 2003/PY
L18 66 S L17 NOT 2002/PY
L19 49 S L18 NOT 2001/PY
L20 38 S L19 NOT 2000/PY
L21 27 S L20 NOT 1999/PY
L22 18 S L21 NOT 1998/PY E KILKUSKIE R/AU
L23 1 S E8 E FRANK B/AU E FRANK B L/AU E FRANK BRUCE/AU
L24 23 S E3 OR E6 OR E7 E GOODCHILD J/AU
L25 75 S E3 OR E10 OR E9 E WOLFE J/AU
L26 41 S E3 E WOLFE J L/AU
L27 2 S E3 E WOLFE JIA/AU
L28 19 S E3 OR E4 OR E5 E ROBERTS P C/AU
L29 6 S E3 E ROBERTS PETER/AU
L30 49 S E3 OR E6 OR E8 E HAMLIN H A/AU
L31 5 S E3 OR E4 OR E10 OR E11 E ROBERTS N A/AU
L32 73 S E2 OR E3 E ROBERTS NOEL/AU
L33 37 S E3 OR E4 OR E5 E WALTHER D M/AU
L34 14 S E3 OR E11

=> s l23 or l24 or l25 or l26 or l27 or l28 or l29 or l30 or l31 or l32 or l33 or l34
L35 317 L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34

=> s l3 and l35
L36 5 L3 AND L35

=> d l36 1-5 bib ab

L36 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:488123 CAPLUS
DN 137:73234
TI Oligonucleotides specific for ***hepatitis*** ***C*** virus treatment
IN ***Kilkuskie, Robert L.*** ; ***Frank, Bruce L.*** ; ***Goodchild,*** *** John*** ; ***Wolfe, Jia L.*** ; ***Roberts, Peter C.*** ; ***Hamlin, Henry A.*** ; ***Roberts, Noel A.*** ; ***Walther, Debra*** *** M.***
PA USA
SO U.S. Pat. Appl. Publ., 74 pp., Cont.-in-part of U.S. Ser. No. 471,968. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 2002081577 A1 20020627 US 1997-887505 19970702
EP 1331267 A2 20030730 EP 2003-5364 19960604
EP 1331267 A3 20031203 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1995-471968 A2 19950606
US 1996-21104P P 19960702
EP 1996-920788 A3 19960604

AB The invention discloses synthetic oligonucleotides complementary to contiguous and non-contiguous regions of the ***HCV*** RNA. Also disclosed are methods and kits for inhibiting the replication of ***HCV*** , inhibiting the expression of ***HCV*** nucleic acid and protein, and for treating ***HCV*** infections.

L36 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:471834 CAPLUS
DN 133:86096
TI Enhancement of ribozyme catalytic activity with 2'-O-substituted facilitator oligonucleotide
IN ***Goodchild, John***
PA University of Massachusetts Worcester, USA
SO U.S., 15 pp., 5612469 Cont.-in-part of U.S. 5,612,469. CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE

PI US 6087484 A 20000711 US 1997-819942 19970318
US 5612469 A 19970318 US 1995-431625 19950501
PRAI US 1992-830713 B1 19920204
US 1993-138896 B1 19931019
US 1995-431625 A2 19950501
AB Methods are disclosed for increasing ribozyme catalytic activity without reducing specificity, which methods comprise contacting an RNA mol. with a ribozyme and a 2'-O-substituted facilitator oligonucleotide. The facilitator oligonucleotide binds to the substrate RNA at a site contiguous to the ribozyme binding site. The present invention further provides compns. comprising a ribozyme and an effective amt. of a 2'-O-Me substituted facilitator oligonucleotide. The use of a facilitator, particularly a 2'-O-substituted facilitator, and more esp. a 2'-O-Me substituted facilitator, greatly enhances ribozyme catalytic activity, frequently making an otherwise inactive ribozyme active. The method was demonstrated with ribozymes targeted to HIV-1 and ***hepatitis*** ***C*** virus RNAs as well as to VEGF mRNA. Both length and presence/absence of 2'-O-Me groups in the oligoribonucleotide facilitator affected the efficiency of substrate cleavage.
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:290674 CAPLUS
DN 127:23730
TI Efficient removal of viruses by a novel polyvinylidene fluoride membrane filter
AU ***Roberts, Peter***
CS Res. & Development Dep., Bio Products Lab., Herts, WD6 3BX, UK
SO Journal of Virological Methods (1997), 65(1), 27-31 CODEN: JVMEDH; ISSN: 0166-0934
PB Elsevier
DT Journal
LA English
AB Virus removal by a novel filter (Ultipor VF DV50), comprising 3 layers of PVDF membrane, was evaluated by infectivity studies using a range of viruses and conditions. The filter was able to remove at least 6 log of various viruses, i.e., Sindbis and Semliki Forest (40-70 nm), herpes simplex (120-200 nm), and vaccinia (200 x 350 nm), from cell-culture medium or phosphate-buffered saline, pH 6.8, contg. 0.5% albumin. However, the removal of

polio virus (25-30 nm) under these conditions was only limited, i.e., about 1 log. This filter is thus effective for removing viruses of about 50 nm or larger. Proteins as large as Igs (MW 160, 000), were able to pass through the filter with recoveries of at least 85%. Due to its ability to remove viruses of medium-to-large size, this filter shows potential for increasing the safety of biol. products where viruses such as hepatitis B, C, herpes, and retroviruses are of concern.
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:124382 CAPLUS
DN 126:126887
TI ***Hepatitis*** ***C*** virus-complementary oligonucleotides and analogs and their use in prophylaxis, treatment and diagnosis of viral infection
IN ***Frank, Bruce L.*** ; ***Goodchild, John*** ; ***Hamlin, Henry***
*** A., Jr.*** ; Kilkuskie, Robert E.; ***Roberts, Noel A.*** ; ***Roberts, Peter C.*** ; ***Walther, Debra M.*** ; ***Wolfe, Jia***
*** L.***
PA F. Hoffmann-La Roche Ag, Switz.; Hybridon Inc.
SO PCT Int. Appl., 99 pp. CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE ---------- ---- -------- ---------- -------
PI WO 9639500 A2 19961212 WO 1996-EP2427 19960604 WO 9639500 A3 19970313 W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG ZA 9604446 A 19961206 ZA 1996-4446 19960530 CA 2226438 AA 19961212 CA 1996-2226438 19960604 AU 9662219 A1 19961224 AU 1996-62219 19960604 EP 833902 A2 19980408 EP 1996-920788 19960604 EP 833902 B1 20030514 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI AT 240392 E 20030515 AT 1996-920788 19960604 EP 1331267 A2 20030730 EP 2003-5364 19960604 EP 1331267 A3 20031203 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI PT 833902 T 20030930 PT 1996-920788 19960604 ES 2196157 T3 20031216 ES 1996-920788 19960604
PRAI US 1995-471968 A 19950606 EP 1996-920788 A3 19960604 WO 1996-EP2427 W 19960604
AB The present invention discloses synthetic oligonucleotides and oligonucleotide analogs complementary to contiguous and non-contiguous regions of the ***hepatitis*** ***C*** virus (***HCV***) RNA. Also disclosed are methods and kits for inhibiting the replication of ***HCV*** , inhibiting the expression of ***HCV*** nucleic acid and protein, and for treating ***HCV*** infections. Numerous oligodeoxyribonucleotides, hybrid oligodeoxy- and deoxyribonucleotides, and analogs of these oligonucleotides contg. modified linkages, modified bases, modified sugar residues, etc. were prepd. These oligonucleotides were tested in RNase H cleavage assays as well as in inhibition of ***HCV*** luciferase fusion protein expression in stably transfected cells, inhibition of ***HCV*** RNA expression in stably transfected cells, and inhibition of ***HCV*** protein expression in Semliki Forest virus/ ***HCV*** recombinant virus infected cells. Sequence-specific inhibition was obsd.

L36 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:569922 CAPLUS
DN 123:28287
TI An in vitro assay for ***hepatitis*** ***C*** virus NS3 serine proteinase
AU Bouffard, Pascal; Bartenschlager, Ralf; Ahlborn-Laake, Ludwina; Mous, Jan; ***Roberts, Noel*** ; Jacobsen, Helmut
CS Antiviral Biol. Dept., Roche Products, Ltd., Herts, AL7 3AY, UK
SO Virology (1995), 209(1), 52-9 CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB ***Hepatitis*** ***C*** virus (***HCV***) encodes a polyprotein of which the majority of nonstructural proteins are matured by the viral serine proteinase located in the N terminus of NS3. Intracellular studies using recombinant vaccinia virus have shown that both NS3 and its cofactor NS4A are required to enhance processing at the NS3-dependent cleavage sites. We developed an in vitro (cell-free) assay in which the ***HCV*** serine proteinase was shown to be enzymically active, by mixing lysates of cells expressing either the serine proteinase or a nonstructural protein substrate. NS3 cleaved in a highly reproducible manner at the NS5A/5B site in the presence of NS4A, whereas NS3 alone was enzymically inactive. NS4A could be provided either linked to NS3 or as part of the substrate. In contrast, irresp. of the presence or absence of NS4A, no NS3-mediated processing was obsd. at the NS3/4A, NS4A/4B, and NS4B/5A sites in this assay. In vitro cleavage at the NS5A/5B site occurred rapidly, within 1 min at temps. ranging from 0 to 20.degree., but was incomplete and required detergent-solubilized lysates. General serine proteinase inhibitors did not decrease processing activity. The in vitro model described in this study is a new tool: (1) to study the structure and the function of ***HCV*** serine proteinase and NS5A/5B cleavage site, and (2) to test NS3 serine proteinase inhibitors.

=> d his
(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005
L1 9043 S HCV/BI,AB
L2 13330 S (HEPATITIS(W)C)/BI,AB
L3 13947 S L1 OR L2
L4 10 S ODN3/BI,AB
L5 75023 S OLIGONUCLEOTIDE#/BI,AB
L6 7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7 9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB
L8 82587 S L4 OR L5 OR L6 OR L7
L9 596 S L3 AND L8
L10 38114 S ANTISENSE/BI,AB
L11 1297 S (ANTI(W)SENSE)/BI,AB
L12 38918 S L10 OR L11
L13 19463 S L8 AND L12
L14 166 S L9 AND L12
L15 136 S L14 NOT 2005/PY
L16 99 S L15 NOT 2004/PY
L17 82 S L16 NOT 2003/PY
L18 66 S L17 NOT 2002/PY
L19 49 S L18 NOT 2001/PY

```
L20         38 S L19 NOT 2000/PY
L21         27 S L20 NOT 1999/PY
L22         18 S L21 NOT 1998/PY          E KILKUSKIE R/AU
L23          1 S E8          E FRANK B/AU          E FRANK B L/AU
E FRANK BRUCE/AU
L24         23 S E3 OR E6 OR E7          E GOODCHILD J/AU
L25         75 S E3 OR E10 OR E9          E WOLFE J/AU
L26         41 S E3          E WOLFE J L/AU
L27          2 S E3          E WOLFE JIA/AU
L28         19 S E3 OR E4 OR E5          E ROBERTS P C/AU
L29          6 S E3          E ROBERTS PETER/AU
L30         49 S E3 OR E6 OR E8          E HAMLIN H A/AU
L31          5 S E3 OR E4 OR E10 OR E11          E ROBERTS N
A/AU
L32         73 S E2 OR E3          E ROBERTS NOEL/AU
L33         37 S E3 OR E4 OR E5          E WALTHER D M/AU
L34         14 S E3 OR E11
L35        317 S L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
L29 OR L30 OR L31 O
L36          5 S L3 AND L35

=> log y
COST IN U.S. DOLLARS                      SINCE FILE
TOTAL                                    ENTRY    SESSION
FULL ESTIMATED COST                         173.00     173.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE
FILE      TOTAL                                    ENTRY
SESSION
CA SUBSCRIBER PRICE                        -16.79     -16.79

STN INTERNATIONAL LOGOFF AT 16:51:51 ON 27 APR 2005
```